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=> file casreact
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FILE CONTENT:1840 - 13 Feb 2005 VOL 142 ISS 7

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*     CASREACT now has more than  8 million reactions      *
*                                                          *
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provided by InfoChem, INPI data prior to 1986, and Biotransformations
database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance
identification.

=> d que
L1            30 SEA FILE=CASREACT LANSOPRAZOLE
L2             1 SEA FILE=CASREACT L1 AND PURIFIC?


=> d l2 ibib abs fcrd


L2   ANSWER 1 OF 1  CASREACT  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         137:263030  CASREACT
TITLE:                    Process for the preparation and purification
                          of antiulcer agent lansoprazole
INVENTOR(S):              Kim, Wan Joo; Kim, Kyoung Soo; Kim, Myung Hwa; Baek,
                          Yong Gu; Park, Jong Yek; Jang, Jung Min; Choi, Jae
                          Won; Yoo, Yong Sang
PATENT ASSIGNEE(S):       Chemtech Research Incorporation, S. Korea; Hansol
                          Chemience Co., Ltd.
SOURCE:                   PCT Int. Appl., 22 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
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     WO 2002074766      A1   20020926      WO 2002-KR261    20020220
         W:  JP, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, TR
     KR 2002068592      A    20020828      KR 2001-8677     20010221
     EP 1368338         A1   20031210      EP 2002-700866   20020220
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI, CY, TR
     JP 2004525927      T2   20040826      JP 2002-573775   20020220
PRIORITY APPLN. INFO.:                     KR 2001-8677     20010221
                                           WO 2002-KR261    20020220
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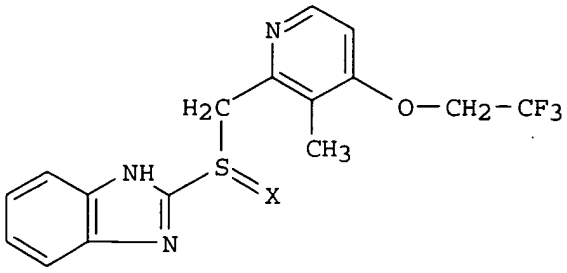

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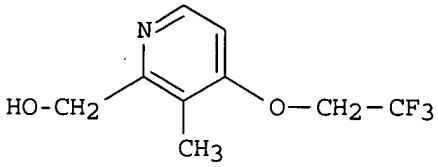

II

AB A process for the preparation of **lansoprazole** I (X = O) comprising of 2-steps: condensation of pyridine II or its salt with 2-mercaptobenzimidazole in the presence of a halogenating agent and oxidation of sulfide I (X = absent) with hydrogen peroxide in the presence of benzeneseleninic acid as a catalyst is disclosed. For example, to a suspension of sulfide I (X = absent, 4.24 mmol), prepared from pyridine II and 2-mercaptobenzimidazole in 1-step, and benzeneseleninic acid (0.0106 mmol) in CH2Cl2 (30 mL) was added tert-butanol (2 mL) and 35.7% hydrogen peroxide (4.46 mmol) at a temperature below 10 °C. After completion of the reaction, the reaction mixture was cooled to 5 °C, and an aqueous solution of Na2S2O3 (0.4 g/20 mL) added at a temperature below 10 °C. The mixture was vigorously stirred for 30 min., the organic layer separated, washed with water (20 mL), dried over anhydrous Mg2SO4, and concentrated under reduced pressure to afforded after recrystn. **lansoprazole** in 95% yield. The present process minimizes the production of 2-[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methylsulfinyl-1H-benzimidazole N-oxide byproduct by a simple and economic oxidation method. **Lansoprazole** is well known as a major component of an anti-ulcer agent having excellent gastric acid secretion inhibiting action and gastric mucous membrane protecting action.

NO HIGHLIGHTING INFORMATION PRESENT

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l1 1-30 ibib abs fcrd

L1 ANSWER 1 OF 30 CASREACT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 141:366231 CASREACT

TITLE: An improved process for manufacture of substituted benzimidazoles via Raney nickel-catalyzed hydrogenation for preparation of antiulcer agents

INVENTOR(S): Vyas, Ketan Dhansukhal; Singh, Dharmendra; Nandavadekar, Sanjay; Bhise, Sanjay; Jadhav, Atul; Desai, Hemal

PATENT ASSIGNEE(S): Ipca Laboratories Limited, India

SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004092142	A1	20041028	WO 2003-IN314	20030917

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IN 2003-MU382 20030417
OTHER SOURCE(S): MARPAT 141:366231
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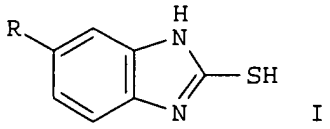

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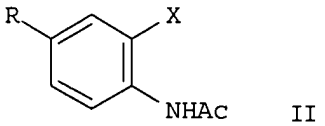


II

AB The invention provides a process for the preparation of mercaptobenzimidazoles I (R = OMe or OCHF2) via hydrogenation of compds. II (X = NO2) in the presence of Raney nickel to the corresponding amines II (X = NH2) followed by treatment with CS2 in the presence of KOH. The use of Raney nickel as catalyst instead of previously reported palladium not only gave high purity of the amines, but also it is cost effective. In the second step, potassium Et xanthate salt, formed from the reaction of carbon disulfide with the base, was suggested to act as cyclizing agent and permit the cyclization and subsequent deacetylation of the generated intermediate simultaneously in one pot, making the process simple and efficient. E.g., p-anisidine was N-acylated with acetic anhydride followed by nitration with nitric acid to afford II (R = OMe, X = NO2). This compound underwent Raney nickel-catalyzed hydrogenation, and subsequent reaction of the resulting amine II (R = OMe, X = NH2) with CS2 in the presence of KOH furnished I (R = OMe). Compds. I are key intermediates in the synthesis of H+/K+-ATPase irreversible inhibitors, such as omeprazole, **lansoprazole**, pantoprazole and rabeprazole.
NO HIGHLIGHTING INFORMATION PRESENT

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

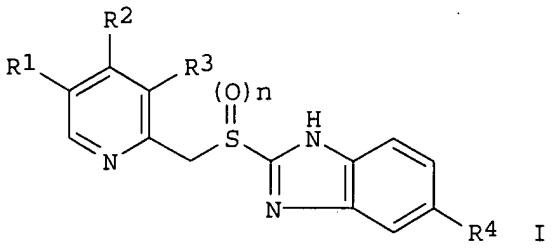
L1 ANSWER 2 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:140445 CASREACT
TITLE: Method for the preparation of pyridinylmethylsulfinylbenzimidazoles which are substantially free of oxidation contaminants for use in pharmaceutical compositions for treatment of gastric ulcers
INVENTOR(S): Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra; Srinivas, Pathi L.
PATENT ASSIGNEE(S): Cipla Limited, India; Wain, Christopher Paul

SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004063188	A1	20040729	WO 2004-GB64	20040112

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ

PRIORITY APPLN. INFO.: IN 2003-MU58 20030115
IN 2003-MU193 20030214
OTHER SOURCE(S): MARPAT 141:140445
GI



I

AB A process was disclosed for the preparation of sulfinylbenzimidazoles, such as I [R1, R3 = H, Me, alkoxy; R2 = alkoxy; R4 = H, alkoxy; n = 1] free of oxidation contaminants, via oxidation of the corresponding sulfenylbenzimidazoles I (n = 0)using metal hypohalites for therapeutic use in pharmaceutical compns. for the treatment of gastric ulcers. Thus, the sodium salt of rabeprazole I [R1 = H, R2 = O(CH2)3OMe, R3 = H, n = 1] was prepared via oxidation of the corresponding sulfenylbenzimidazole I [R1 = H, R2 = O(CH2)3OMe, R3 = H, n = 0] using a 3.8% sodium hypochlorite solution, sodium hydroxide and pyridine in water.
NO HIGHLIGHTING INFORMATION PRESENT

L1 ANSWER 3 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:116452 CASREACT
TITLE: Chemistry of Covalent Inhibition of the Gastric (H+, K+)-ATPase by Proton Pump Inhibitors
AUTHOR(S): Shin, Jai Moo; Cho, Young Moon; Sachs, George
CORPORATE SOURCE: Department of Physiology and Medicine, University of California, Los Angeles, CA, 90073, USA
SOURCE: Journal of the American Chemical Society (2004), 126(25), 7800-7811
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Proton pump inhibitors (PPIs), drugs that are widely used for treatment of acid related diseases, are either substituted pyridylmethylsulfinyl

benzimidazole or imidazopyridine derivs. They are all prodrugs that inhibit the acid-secreting gastric (H+, K+)-ATPase by acid activation to reactive thiophiles that form disulfide bonds with one or more cysteines accessible from the exoplasmic surface of the enzyme. This unique acid-catalysis mechanism had been ascribed to the nucleophilicity of the pyridine ring. However, the data obtained here show that their conversion to the reactive cationic thiophilic sulfenic acid or sulfenamide depends mainly not on pyridine protonation but on a second protonation of the imidazole component that increases the electrophilicity of the C-2 position on the imidazole. This protonation results in reaction of the C-2 with the unprotonated fraction of the pyridine ring to form the reactive derivs. The relevant PPI pKa's were determined by UV spectroscopy of the benzimidazole or imidazopyridine sulfinylmethyl moieties at different medium pH. Synthesis of a relatively acid stable analog, N1-Me **lansoprazole**, allowed direct determination of both pKa values of this intact PPI allowing calcn. of the two pKa values for all the PPIs. These values predict their relative acid stability and thus the rate of reaction with cysteines of the active proton pump at the pH of the secreting parietal cell. The PPI accumulates in the secretory canaliculus of the parietal cell due to pyridine protonation then binds to the pump and is activated by the second protonation on the surface of the protein to allow disulfide formation.

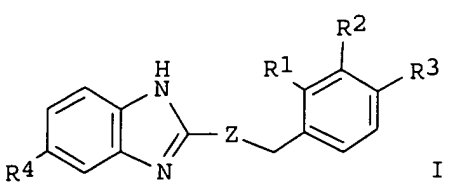
NO HIGHLIGHTING INFORMATION PRESENT

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 4 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:106473 CASREACT
TITLE: Processes for the production of substituted 2-(2-pyridylmethyl) sulfinyl-1H-benzimidazoles
INVENTOR(S): Avrutov, Ilya; Mendelovici, Marioara; Finkelstein, Nina
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 8 pp., Cont.-in-part of U.S. Ser. No. 66,850.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004138466	A1	20040715	US 2003-655645	20030904
US 2003036554	A1	20030220	US 2002-66850	20020204
PRIORITY APPLN. INFO.:			US 2001-266162P	20010202
			US 2002-66850	20020204
			US 2002-408163P	20020904

OTHER SOURCE(S): MARPAT 141:106473
GI



I

AB The present invention discloses improved processes for preparing substituted 2-(2-pyridylmethyl)sulfinyl-1H-benzimidazoles, such as I [R1, R2, R4 = H, alkyl, alkoxy; R3 = H, alkyl; Z = SO], via selective oxidation of a thioether compound II (Z = S), with an oxidizing agent selected from the group consisting of tert-Bu hydroperoxide in the presence of a catalyst, vanadium acetylacetonate, oxone and potassium peroxymonosulfate.
NO HIGHLIGHTING INFORMATION PRESENT

L1 ANSWER 5 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:357338 CASREACT
TITLE: Preparation of sulfinyl-containing drugs by catalytic oxidation of thioether compounds
INVENTOR(S): Yang, Guangzhong
PATENT ASSIGNEE(S): Institute of Pharmacy, Chinese Academy of Medical Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 12 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1381443	A	20021127	CN 2001-109783	20010420

PRIORITY APPLN. INFO.: CN 2001-109783 20010420

AB The thioether compds., such as 5-methoxy-2-(3,5-dimethyl-4-methoxy-2-pyridylmethylthio)-1H-benzimidazole, 2-[3-methyl-4--2-pyridylmethylthio]-1H-benzimidazole, 5-difluoromethoxy-2-(3,4-dimethoxy-2-pyridylmethylthio)-1H-benzimidazole, 2-[4-(3-methoxypropoxy)-3-methyl-2-pyridylmethylthio]-1H-benzimidazole, or (diphenylmethyl)thioacetamide, were oxidized to sulfoxide by using tert-Bu hydroperoxide (tert-Bu hypochlorite, NaClO, H2O2, perbenzoic acid, or 3-chloroperbenzoic acid) in nonprotic solvent (such as dichloromethane, chloroform, CCl4, acetone, Et acetate, etc) in the presence of catalyst (0.5-10%) at 0-25°. The catalyst is titanium tetraisopropoxide, bis(pentane-2,4-dionato)vanadium oxide, bis(pentane-2,4-dionato)copper(II), bis(pentane-2,4-dionato)cobalt(II), tris(pentane-2,4-dionato)iron(III), bis(pentane-2,4-dionato)manganese(II), or tris(pentane-2,4-dionato)chromium(III).
NO HIGHLIGHTING INFORMATION PRESENT

L1 ANSWER 6 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:146140 CASREACT
TITLE: Preparation of **lansoprazole** and related compounds
INVENTOR(S): Finkelstein, Nina
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004011455	A1	20040205	WO 2003-US23588	20030728

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1467987 A1 20041020 EP 2003-748985 20030728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.: US 2002-398686P 20020726
WO 2003-US23588 20030728

OTHER SOURCE(S): MARPAT 140:146140

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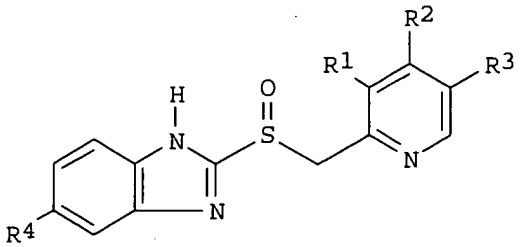

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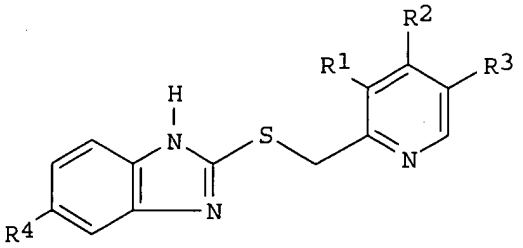


II

AB The present invention provides a process for preparing **lansoprazole** (LNP) and related compds. I (R1, R2, R4 = H, alkyl, alkoxy; R3 = H, alkyL) having a high yield and a low level of impurities by oxidation of corresponding sulfides II with tert-Bu hydroperoxide (TBHP), catalyzed by a catalyst vanadium oxytrichloride in an organic solvent selected from the group consisting of a C1-C5 alkanol, decane, nonane, toluene and a mixture of the organic solvent and water, preferably in the presence of a base. Thus, oxidation of 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-1H-benimidazole with TBPH in isopropanal in the presence of Et2NH and VOCl3 at 10° for 16 h gave 90% **lansoprazole.**

NO HIGHLIGHTING INFORMATION PRESENT

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 7 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:111413 CASREACT
TITLE: Preparation of Mg salt of [(substituted

pyridyl)methyl]sulfinyl-1H-benzimidazole derivatives
INVENTOR(S): Cui, Mingquan; He, Chuanhua; Wang, Xiaoling; Li, Lan; Peng, Jiankun; Qiu, Yu
PATENT ASSIGNEE(S): Chengdu Yaoyou Science and Technology Development Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1367172	A	20020904	CN 2002-113294	20020130
PRIORITY APPLN. INFO.:			CN 2002-113294	20020130

AB The Mg salts of [(substituted pyridyl)methyl]sulfinyl-1H-benzimidazole derivs. are prepared by the reaction of [(substituted pyridyl)methyl]sulfinyl-1H-benzimidazole derivs. with soluble Mg salt (such as MgCl2 or Mg(NO3)2) (at a molar ratio of 1:0.45- 0.55) in alkaline solution at pH 9-13.
NO HIGHLIGHTING INFORMATION PRESENT

L1 ANSWER 8 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:59642 CASREACT
TITLE: preparation of almost anhydrous **lansoprazole** from its solvate and/or hydrate
INVENTOR(S): Aihara, Kiyoshi; Hiroshige, Eiko; Yokogoshi, Kiyonori
PATENT ASSIGNEE(S): Permachem Asia, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp. CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004002230	A2	20040108	JP 2002-160105	20020531
PRIORITY APPLN. INFO.:			JP 2002-160105	20020531

AB Almost anhydrous **lansoprazole** (I, already know as antiulcer agent) is prepared by dissolving solvate and/or hydrate of I in solvent, crystallizing by aqueous alkali, and drying at low temperature Thus, I hydrate (H2O content 1.5%) was dissolved in DMF, treated with ammonia at pH 9, filtered, and dried at 40° for 12 h to give white I crystals, which contained 0.04% H2O.
NO HIGHLIGHTING INFORMATION PRESENT

L1 ANSWER 9 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 139:395935 CASREACT
TITLE: New method for the preparation of the anti-ulcer compounds omeprazole, **lansoprazole** and pantoprazole
INVENTOR(S): Correia, Pedro Brito; Romao, Carlos Crispim; Correia, Luis Brito; Pereira, Maria Florbela; Fernandes, Ana Cristina; Borges, Jose Enrique; Tavares, Regina; Costa, Maria Do Ceu; Teixeira, Fatima
PATENT ASSIGNEE(S): Herbex, Produtos Quimicos Sa, Port.; Saragga, Jose

Manuel
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097606	A1	20031127	WO 2000-IB1057	20000728

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2000-IB1057 20000728
OTHER SOURCE(S): MARPAT 139:395935

AB The present invention describes a new process for the intermediate preparation of omeprazole, **lansoprazole** and pantoprazole , and which involves the formation of pyridines N-oxide using a rhenium compound as a catalyst, followed by nitration of the 4-position with nitric acid fuming in presence of a claycop. The chlorination of the 2-Me group of pyridine was achieved by using the POCl3/Et3N, which allowed the preparation of the derivs. 2-chloromethylpyridines in only one step. These derivs. reacted with the mercaptobenzimidazolic derivs. in presence of ultra-sonic radiation, giving the thioethers. The oxidation of these thioethers was done with several oxidizing agents and the required anti-ulcer compds. were obtained after the substitution of nitro group by the corresponding OR groups. Thus, Omeprazole was prepared by oxidation of 2,3,5-colidine with hydrogen peroxide in presence of methyltrioxorhenium catalyst; nitration; chlorination to form 2-chloromethyl-3,5-dimethyl-4-nitropyridine; reaction with 5-methoxy-2-mercaptobenzimidazole; oxidation; and reaction with sodium methoxide.

NO HIGHLIGHTING INFORMATION PRESENT
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 10 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 139:149633 CASREACT
TITLE: A method for eliminating sulfone formation in the synthesis of pyridine-benzimidazole sulfoxides
INVENTOR(S): Uensal, Serafettin
PATENT ASSIGNEE(S): Ulkar Kimya Sanayii Ve Ticaret Anonim Sirketi, Turk.
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062223	A1	20030731	WO 2002-TR58	20021001

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1476441 A1 20041117 EP 2002-806580 20021001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
PRIORITY APPLN. INFO.: TR 2002-186 20020123
WO 2002-TR58 20021001
OTHER SOURCE(S): MARPAT 139:149633
AB A process is described for the elimination of sulfone analogs in contaminated pyridine-benzimidazole sulfoxide products. The purification process comprises treatment of semi-pure benzimidazole derivs. [e.g., 2-[[3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl]methylsulfinyl]benzimidazole] with solid K2CO3 in alc. medium (e.g., aqueous ethanol) at elevated temps. and by oxidation of the corresponding thioether [e.g., 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl]methyl]thio]benzimidazole] with peracids (e.g., m-chloroperbenzoic acid).
NO HIGHLIGHTING INFORMATION PRESENT
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 11 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:368576 CASREACT
TITLE: WO3-30% H2O2-cinchona alkaloids: a new heterogeneous catalytic system for the asymmetric oxidation of sulfides and the kinetic resolution of racemic sulfoxides
AUTHOR(S): Thakur, Vinay V.; Sudalai, A.
CORPORATE SOURCE: Process Development Division, National Chemical Laboratory, Pune, 411008, India
SOURCE: Tetrahedron: Asymmetry (2003), 14(4), 407-410
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB WO3-catalyzed asym. oxidation of thioethers and kinetic resolution of sulfoxides
with 30% aqueous H2O2 in the presence of cinchona alkaloids under heterogeneous conditions affords chiral sulfoxides in high yields with moderate to good enantioselectivities. For example, the oxidation of 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]thio]-1H-Benzimidazole with hydrogen peroxide in the presence of tungsten oxide (WO3) and (DHQD)2-PYR gave 2-[(R)-[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-1H-Benzimidazole [(R)-(+)-**lansoprazole**].
NO HIGHLIGHTING INFORMATION PRESENT
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 12 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:205056 CASREACT
TITLE: Preparation of optically pure **lansoprazole**
INVENTOR(S): Deng, Jingen; Peng, Xiaohua; Cui, Xin; Fu, Fangmin; Zhu, Jin; Chi, Yongxiang; Jiang, Yaozhong
PATENT ASSIGNEE(S): Chengdu Inst. of Organic Chemistry, Chinese Academy of

Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 20 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1329003	A	20020102	CN 2000-113036	20000619
CN 1117747	B	20030813		
PRIORITY APPLN. INFO.:			CN 2000-113036	20000619

AB **Lansoprazole** is optically resolved by allowing to react with chiral binaphthol (at a molar ratio of 1:2-6) in organic solvent for 12-72 h, standing at 10-30° for 5-48 h, filtering to inclusion compound with one optical configuration, separating **lansoprazole** and binaphthol from the inclusion compound on chromatog. column to obtain oily or syrup **lansoprazole**; treating with 1-10% inorg. base solution at 50-120° for 5 min-2 h to pH 10-13 to obtain colorless or light yellow **lansoprazole** solution; cooling in ice-salt bath for 1-3 h and at -20 to 10° for 5-20 h to obtain white amorphous solid of **lansoprazole**; and recrystg. to obtain white crystal of **lansoprazole.**
NO HIGHLIGHTING INFORMATION PRESENT

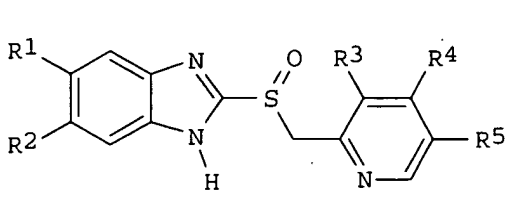
L1 ANSWER 13 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:137309 CASREACT
TITLE: Improved process for preparing benzimidazole-type compounds, particularly antiulcer agents such as rabeprazole, by oxidation of sulfide analogs and controlled pH alkaline extraction to remove sulfone impurities
INVENTOR(S): Broeckx, Rudy Laurent Maria; De Smaele, Dirk; Leurs, Stefan Marcel Herman
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008406	A1	20030130	WO 2002-EP7693	20020709
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EE 200400052	A	20040415	EE 2004-52	20020709
EP 1409478	A1	20040421	EP 2002-754865	20020709
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

BR 2002011101	A	20040622	BR 2002-11101	20020709
NZ 530168	A	20040827	NZ 2002-530168	20020709
JP 2005500333	T2	20050106	JP 2003-513965	20020709
US 2004209918	A1	20041021	US 2004-483587	20040604
PRIORITY APPLN. INFO.:			EP 2001-202696	20010716
			WO 2002-EP7693	20020709

OTHER SOURCE(S): MARPAT 138:137309

GI



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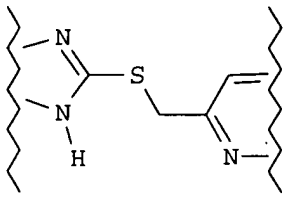
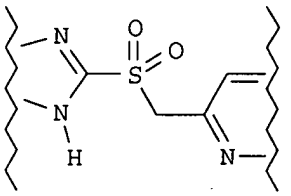
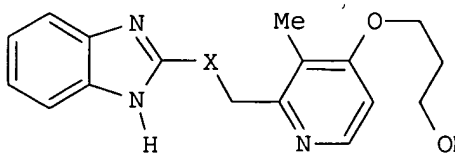


II



III



IV

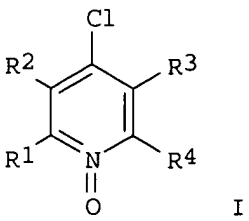
AB The invention relates to an improved process for the preparation of benzimidazole-type proton pump inhibitors, including the antiulcer agents rabeprazole, omeprazole, pantoprazole, **lansoprazole**, and esomeprazole. The method provides for efficient removal of sulfone impurities in the oxidative production of these sulfoxide drugs. Specifically, the method concerns preparation of sulfoxides I [R1, R2 = H, OMe, OCHF2; R3, R4, R5 = H, Me, OMe, methoxypropoxy, trifluoroethoxy] by oxidation of the corresponding sulfides II, followed by extraction of the sulfone byproducts III with an aqueous alkaline solution at controlled pH. In particular, the reaction mixture is extracted with an aqueous alkaline solution of pH 9.50-12.00, and the aqueous layer containing III is removed. The organic layer is then extracted with an aqueous alkaline solution of pH 13.0 or higher, and the organic layer containing impurities is removed. Finally, sulfoxides I are isolated from the aqueous layer. By more efficiently removing the sulfone, the method allows for use of higher amts. of oxidizing agent, leading to increased yields. For example, the sulfide precursor of rabeprazole, IV (X = S), was oxidized with 0.88 equiv m-CPBA in CH2Cl2 at -20° over 1.5 h. The reaction mixture was diluted. with H2O and the pH adjusted to 10.40 with 10% NaOH, then to 10.85 with aqueous NH3. The aqueous layer (sulfone) was removed, and the organic layer was treated with H2O and the pH raised to 13.0 with 10% NaOH. The organic layer (impurities) was removed, and the aqueous layer (sulfoxide) was treated with CH2Cl2 and adjusted to pH 10.5 with aqueous NH4OAc. The organic layer (sulfoxide) was removed and concentrated, and the residue crystallized from acetone to give rabeprazole, i.e., IV (X = SO) in 57% yield. In contrast, a similar, standard preparation of rabeprazole, using 0.60 equiv m-CPBA and a single

extraction at pH 13.0, gave only 44% yield. In both cases, the level of sulfone IV (X = SO2), ≤ 0.8%, was pharmaceutically acceptable. In another experiment, sulfone levels were compared in the prepns. of 3 drugs (new/standard): rabeprazole 0.33%/0.78%, omeprazole 0.26%/0.53%, and **lansoprazole** 4.1%/11.3% (sic).
NO HIGHLIGHTING INFORMATION PRESENT
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 14 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:39192 CASREACT
TITLE: Regioselective chlorination process for the preparation of 4-chloropyridine-N-oxides
INVENTOR(S): De Bode, Ronus; Liebregts, Constantinus Simon Maria; Zwaan, Wilhelmus
PATENT ASSIGNEE(S): DSM N.V., Neth.
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102779	A1	20021227	WO 2002-NL379	20020611
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
NL 1018295	C2	20021217	NL 2001-1018295	20010615

PRIORITY APPLN. INFO.: NL 2001-1018295 20010615
OTHER SOURCE(S): MARPAT 138:39192
GI



I

AB 4-Chloropyridine-N-oxides (I; R1-R3 = H, alkyl, alkoxy; R4 = alkyl, alkoxy; e.g., 4-chloro-2,3-dimethylpyridine-N-oxide) are prepared in high yield and selectivity by the regioselective chlorination of the corresponding 4-H-pyridine-N-oxides (e.g., 2,3-dimethylpyridine-N-oxide) with Cl2. I are intermediates used in the preparation of pharmaceuticals, for example omeprazole, pantoprazole, rabeprazole, and **lansoprazole** (no data).
NO HIGHLIGHTING INFORMATION PRESENT

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 15 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 137:263030 CASREACT
TITLE: Process for the preparation and purification of antiulcer agent **lansoprazole**
INVENTOR(S): Kim, Wan Joo; Kim, Kyoung Soo; Kim, Myung Hwa; Baek, Yong Gu; Park, Jong Yek; Jang, Jung Min; Choi, Jae Won; Yoo, Yong Sang
PATENT ASSIGNEE(S): Chemtech Research Incorporation, S. Korea; Hansol Chemience Co., Ltd.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002074766	A1	20020926	WO 2002-KR261	20020220
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
KR 2002068592	A	20020828	KR 2001-8677	20010221
EP 1368338	A1	20031210	EP 2002-700866	20020220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2004525927	T2	20040826	JP 2002-573775	20020220
PRIORITY APPLN. INFO.:			KR 2001-8677	20010221
			WO 2002-KR261	20020220

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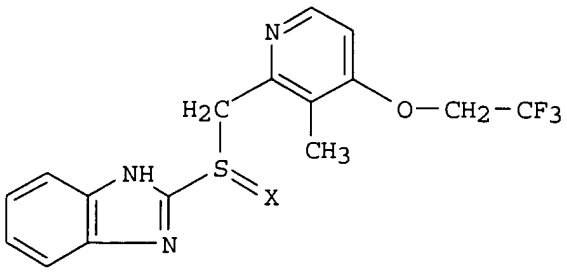
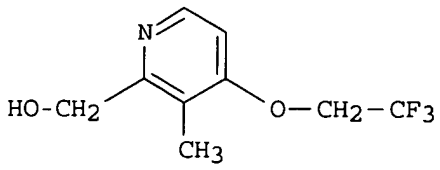


I

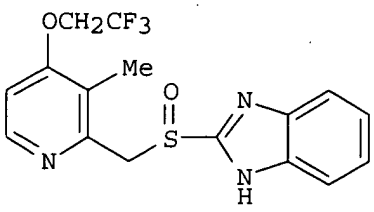


II

AB A process for the preparation of **lansoprazole** I (X = O) comprising of 2-steps: condensation of pyridine II or its salt with 2-mercaptobenzimidazole in the presence of a halogenating agent and oxidation of sulfide I (X = absent) with hydrogen peroxide in the presence of benzeneseleninic acid as a catalyst is disclosed. For example, to a

suspension of sulfide I (X = absent, 4.24 mmol), prepared from pyridine II and 2-mercaptobenzimidazole in 1-step, and benzeneseleninic acid (0.0106 mmol) in CH2Cl2 (30 mL) was added tert-butanol (2 mL) and 35.7% hydrogen peroxide (4.46 mmol) at a temperature below 10 °C. After completion of the reaction, the reaction mixture was cooled to 5 °C, and an aqueous solution of Na2S2O3 (0.4 g/20 mL) added at a temperature below 10 °C. The mixture was vigorously stirred for 30 min., the organic layer separated, washed with water (20 mL), dried over anhydrous Mg2SO4, and concentrated under reduced pressure to afforded after recrystn. **lansoprazole** in 95% yield. The present process minimizes the production of 2-[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methylsulfinyl-1H-benzimidazole N-oxide byproduct by a simple and economic oxidation method. **Lansoprazole** is well known as a major component of an anti-ulcer agent having excellent gastric acid secretion inhibiting action and gastric mucous membrane protecting action.
NO HIGHLIGHTING INFORMATION PRESENT
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 16 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 137:262984 CASREACT
TITLE: A new synthetic process of **lansoprazole**
AUTHOR(S): Ahn, Kwang-Hyun; Kim, Hakwon; Kim, Jeong Ryul; Jeong, Soon Cheol; Kang, Tae Seop; Shin, Hyun Tae; Lim, Geun Jho
CORPORATE SOURCE: College of Environ. and Applied Chem., Yongin City, 449-701, S. Korea
SOURCE: Bulletin of the Korean Chemical Society (2002), 23(4), 626-628
CODEN: BKCSDE; ISSN: 0253-2964
PUBLISHER: Korean Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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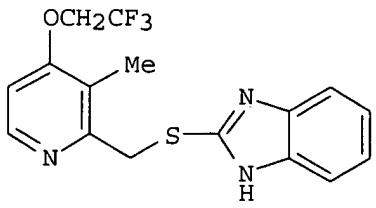


II

AB The proton pump inhibitor, **lansoprazole** (I) has been prepared in eight steps from 3-methyl-4-nitropyridine 1-oxide in 36% overall yield. The key step in the process is the selective oxidation of sulfide II to I using hydrogen peroxide with a heterogeneous catalyst, LiNbMoO6.
NO HIGHLIGHTING INFORMATION PRESENT
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 17 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 137:169521 CASREACT
TITLE: Processes for the production of substituted 2-(2-pyridinylmethyl) sulfinyl-1H-benzimidazoles using tert-butyl hydroperoxide or oxone

INVENTOR(S): Avrutov, Ilya; Mendelovici, Marioara
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceutical USA, Inc.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062786	A1	20020815	WO 2002-US3225	20020204
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2436467	AA	20020815	CA 2002-2436467	20020204
EP 1363901	A1	20031126	EP 2002-706135	20020204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004524303	T2	20040812	JP 2002-563139	20020204
NO 2003003433	A	20030925	NO 2003-3433	20030801
PRIORITY APPLN. INFO.:			US 2001-266162P	20010202
			WO 2002-US3225	20020204

OTHER SOURCE(S): MARPAT 137:169521
AB RZR1 (I; Z = SO) [R = (un)substituted 1H-benzimidazol-2-yl; R1 = (un)substituted 2-pyridinyl] were prepared by selective oxidation of I (Z = S) with tert-Bu hydroperoxide or oxone. Oxidation with tert-Bu hydroperoxide were performed in the presence of VO(acac)2, silica bound V2O5 and NaVO3.
NO HIGHLIGHTING INFORMATION PRESENT
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 18 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 137:93755 CASREACT
TITLE: Preparation of **lansoprazole** via coupling of 2-mercaptobenzimidazole with 2-hydroxymethyl-3-methyl-4-(2,2,2-trifluoroethoxy)pyridine followed by radical oxidation.
INVENTOR(S): Moon, Young-Ho; Lee, Kyung-Ik; Lee, Gwan-Sun
PATENT ASSIGNEE(S): Hanmi Pharm. Co., Ltd., S. Korea
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6423846	B1	20020723	US 2001-967581	20010928
PRIORITY APPLN. INFO.:			US 2001-967581	20010928

AB **Lansoprazole** (I) was prepared by coupling of 2-mercaptobenzimidazole (II) with 2-hydroxymethyl-3-methyl-4-(2,2,2-

trifluoroethoxy)pyridine (III) in the presence of a phosphine and a dialkyl azodicarboxylate followed by treatment of the sulfide intermediate with oxidant in a mixture of water and an organic solvent in the presence of an organic free radical and a phase transfer catalyst. Thus, II, III, and Ph3P in THF were treated dropwise with di-Et azodicarboxylate (DEAD) in THF at room temperature, and stirred for 1 h to give 95% 2-[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methylthio-1H-benzimidazole. The latter with tetramethyl-1-piperidinyloxy (TEMPO) in THF, was combined with tetrabutylammonium chloride in water. The resulting mixture was cooled to 0° and aqueous NaOCl was added over 2 h at 0° followed by stirring for 10 min at 0° and then for 10 min at 20° to give 90% I.
NO HIGHLIGHTING INFORMATION PRESENT
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 19 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:356811 CASREACT
TITLE: Microbial synthesis of a proton pump inhibitor by enantioselective oxidation of a sulfide into its corresponding sulfoxide by Cunninghamella echinulata MK40
AUTHOR(S): Yoshida, Toyokazu; Kito, Mitsuaki; Tsujii, Masahiko; Nagasawa, Toru
CORPORATE SOURCE: Department of Biomolecular Science, Faculty of Engineering, Gifu University, Gifu, 501-1193, Japan
SOURCE: Biotechnology Letters (2001), 23(15), 1217-1222
CODEN: BILED3; ISSN: 0141-5492
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Microbial oxidation of 2-[4-(3-methoxypropoxy)-3-methylpyridin-2-yl]methylthiobenzimidazole to a useful proton pump inhibitor, sodium 2-[[4-(3-methoxypropoxy)-3-methylpyridin-2-yl] methylsulfinyl]-1H benzimidazole (Rabeprazole), was examined in over 650 microorganisms. Rabeprazole-forming activity was distributed in molds. The mold with the highest activity was identified as Cunninghamella echinulata. Glucose, when added to the reaction mixture, gave the highest accumulation of Rabeprazole (6.9 mM, 2.5 g l-1) with a molar conversion ratio of 92% without the formation of the sulfone form as undesired product and resulted in the exclusive formation of (S) enantiomer (>99% e.e.).
NO HIGHLIGHTING INFORMATION PRESENT
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 20 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:331424 CASREACT
TITLE: Method for obtaining derivatives of [[(substituted-pyridyl)methyl]thio]benzimidazole, useful as intermediates for omeprazole and related antiulcer agents
INVENTOR(S): Coppi, Laura; Berenguer Maimo, Ramon
PATENT ASSIGNEE(S): Esteve Quimica, S.A., Spain
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079194	A1	20011025	WO 2001-ES143	20010410
WO 2001079194	C2	20030508		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ES 2171116	A1	20020816	ES 2000-989	20000414
ES 2171116	B1	20030801		
AU 2001046551	A5	20011030	AU 2001-46551	20010410
CA 2405304	AA	20021007	CA 2001-2405304	20010410
JP 2003531144	T2	20031021	JP 2001-576794	20010410
EP 1411053	A1	20040421	EP 2001-919463	20010410
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NZ 521930	A	20040730	NZ 2001-521930	20010410
US 2003036656	A1	20030220	US 2002-204604	20020820
US 6723852	B2	20040420		
NO 2002004858	A	20021206	NO 2002-4858	20021008
PRIORITY APPLN. INFO.:			ES 2000-989	20000414
			WO 2001-ES143	20010410

OTHER SOURCE(S): MARPAT 135:331424
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a method for obtaining derivs. of [[(substituted-pyridyl)methyl]thio]benzimidazoles, i.e., I [wherein R1, R3, R4 = H, C1-6 alkyl, alkoxy, or fluoroalkoxy; R2 = NO2, halo, C1-6 alkoxy or haloalkoxy, or O(CH2)nOR8; n = 1-6; R8 = H or C1-6 alkyl]. The method involves the following steps: (a) reaction of a 2-methylpyridine N-oxide II with a carboxylic acid anhydride (R6CO)2O or a sulfonic acid anhydride (R7SO2)2O [R6 = haloalkyl; R7 = (halo)alkyl or (un)substituted aryl]; and (b) reacting the resultant intermediate III [R5 = OCOR6 or OSO2R7] with a corresponding 2-mercaptobenzimidazole. The compds. I are useful as key intermediates for synthesizing corresponding sulfoxides with known antiulcer activity, e.g., omeprazole, **lansoprazole**, rabeprazole, or pantoprazole. The method offers a reduced number of steps, avoids production of irritating acid chlorides and (chloromethyl)pyridines, and produces fewer residues and byproducts. For instance, reaction of 2,3-dimethyl-4-nitropyridine with (MeSO2)2O in refluxing CHCl3 gave 94% 2-(mesyloxymethyl)-3-methyl-4-nitropyridine methanesulfonate. Reaction of this mesylate with 2-mercapto-1H-benzimidazole and Et3N in CHCl3 at 5-20° gave 82% title compound IV. This intermediate was etherified at the nitro group with CF3CH2OH and K2CO3 (86%), and S-oxidized from the sulfide to the sulfoxide using Na percarbonate and ammonium molybdate catalyst (90%), to give **lansoprazole** (V).

NO HIGHLIGHTING INFORMATION PRESENT

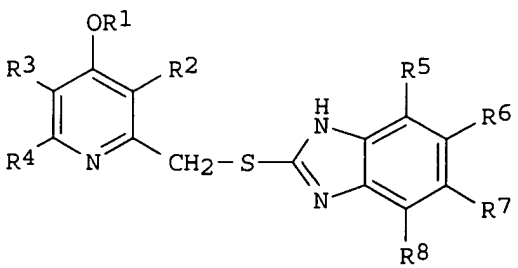
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 21 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:242230 CASREACT
TITLE: Method for oxidizing a thioether group into a sulfoxide group in benzimidazole derivatives
INVENTOR(S): Berenguer Maimo, Ramon; Campon Pardo, Julio; Coppi, Laura
PATENT ASSIGNEE(S): Esteve Quimica, S.A., Spain
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068594	A1	20010920	WO 2001-ES88	20010308
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ES 2163372	A1	20020116	ES 2000-595	20000313
ES 2163372	B1	20030501		
CA 2402635	AA	20010920	CA 2001-2402635	20010308
AU 2001037452	A5	20010924	AU 2001-37452	20010308
EP 1270555	A1	20030102	EP 2001-909846	20010308
EP 1270555	B1	20040825		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003527370	T2	20030916	JP 2001-567691	20010308
NZ 521071	A	20040528	NZ 2001-521071	20010308
AT 274492	E	20040915	AT 2001-909846	20010308
US 2003028030	A1	20030206	US 2002-204506	20020820
US 6603009	B2	20030805		
NO 2002004239	A	20020905	NO 2002-4239	20020905

PRIORITY APPLN. INFO.: ES 2000-595 20000313
WO 2001-ES88 20010308

OTHER SOURCE(S): MARPAT 135:242230
GI



I

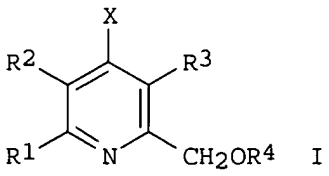
AB The invention concerns a method for oxidizing a thioether group into a sulfoxide group using aqueous sodium percarbonate in the presence of a molybdenum salt as catalyst. The method can be used to oxidize the thioether group in compds. I [R1 = C1-C6 alkyl, halo-C1-C6 alkyl or

(CH2)nOR9 (n = 1-6; R9 = H, C1-C6 alkyl); R2-R6, R8 = H, C1-C6 alkyl, or C1-C6 alkoxy; R7 = H, C1-C6 alkyl, C1-C6 alkoxy or fluoro-C1-C6 alkoxy] to the corresponding sulfinyl compds. Thus, a treating a methanol solution of 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]thio]-1H-benzimidazole with ammonium molybdate and sodium percarbonate and stirring 15 h at 10° afforded 90% sulfoxide (**lansoprazole**).
NO HIGHLIGHTING INFORMATION PRESENT
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 22 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 132:64176 CASREACT
TITLE: Preparation of 2-hydroxymethylpyridine metal complexes as intermediates for pyridinebenzimidazoles.
INVENTOR(S): Nikolopoulos, Angelo; Schickaneder, Helmut; Kocher, Christian; Murphy, Trevor; Hermann, Gesine
PATENT ASSIGNEE(S): Russinsky Limited, Ire.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000474	A1	20000106	WO 1999-IE55	19990618
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DE, DK, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9943877	A1	20000117	AU 1999-43877	19990618
PRIORITY APPLN. INFO.:			IE 1998-514	19980626
			WO 1999-IE55	19990618

OTHER SOURCE(S): MARPAT 132:64176
GI



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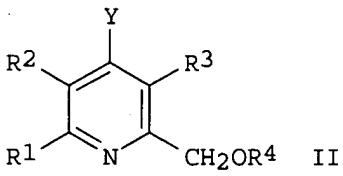


II

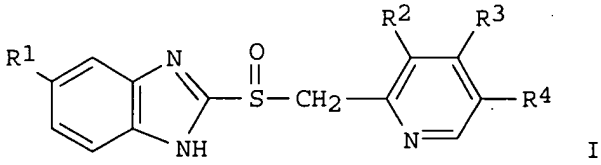
AB IkMzAl(OR5)mSn [R1-R3 = H, alkyl, CF3, CHF2, CH2F, alkoxy, alkoxyalkoxy, OCH2CF3; R4 = H, alkyl, PhCH2, AcO, PhCH2O, trialkylsilyl, neg. charge; R5 = alkyl, aryl, CH2CF3, CF3, CHF2, alkylalkoxy; X = halo, NO2, SO3, OH; M = alkaline earth metal, third main group element, transition metal; S = solvent; k = 1-4; l = 1-3; m = 0-3; n ≥0; z = l+m; with a proviso] and IIkMz(OR5)mSn [Y = alkoxy, aryloxy, OCH2CF3, alkoxyalkoxy, alkylthio, alkylthioalkylthio; z = m; other variables as above], were prepared Thus, 4-nitro-2,3,5-trimethylpyridine N-oxide was heated in HOAc/Ac2O at 20-100° for 1 h to give 88% 2-acetoxymethyl derivative, which was stirred at 10-30° with NaOH in EtOH for 1 h to give 84%

3,5-dimethyl-2-hydroxymethyl-4-nitropyridine (II). II in MeOH was treated with ZnCl2 and with NaOMe in MeOH to give 100% Zn(II)ClOMe.
NO HIGHLIGHTING INFORMATION PRESENT
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 23 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 130:223273 CASREACT
TITLE: Preparation of pyridinylmethylsulfinylbenzimidazoles
INVENTOR(S): Arakawa, Nobuo; Kuroda, Hirofumi
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11071370	A2	19990316	JP 1998-179461	19980626
PRIORITY APPLN. INFO.:			JP 1997-170058	19970626

OTHER SOURCE(S): MARPAT 130:223273
GI



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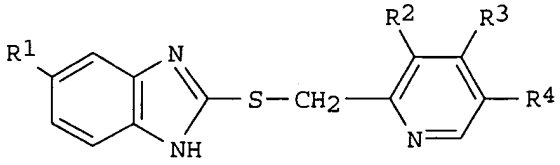


II

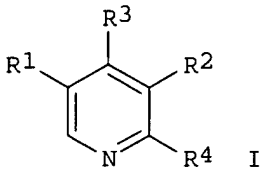
AB Title compds. I (R1 = H, OMe, OCHF2; R2 = Me, MeO; R3 = 3-methoxypropoxy, MeO, CF3CH2O; R4 = H, Me) were prepared by oxidation of thio ethers II (R1-R4 = same as above) with m-chloroperbenzoic acid in nonpolar solvents and lower alcs. Thus, oxidation of 2-{[4-(3-methoxypropoxy)-3-methylpyridin-2-yl]methylthio}-1H-benzimidazole with m-chloroperbenzoic acid in toluene and methanol at -25° for 6.5 h gave 93.1% 2-{[4-(3-methoxypropoxy)-3-methylpyridin-2-yl]methylsulfinyl}-1H-benzimidazole.
NO HIGHLIGHTING INFORMATION PRESENT

L1 ANSWER 24 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 129:343418 CASREACT
TITLE: Synthesis of pyridine derivatives useful as pharmaceutical intermediates under free radical conditions.

INVENTOR(S): Zoghbi, Michel; Chen, Liquin
PATENT ASSIGNEE(S): Pdi-Research Laboratories, Inc., Can.
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9850361	A2	19981112	WO 1998-CA375	19980421
WO 9850361	A3	19990204		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2204580	AA	19981106	CA 1997-2204580	19970506
AU 9870220	A1	19981127	AU 1998-70220	19980421
PRIORITY APPLN. INFO.:			CA 1997-2204580	19970506
			WO 1998-CA375	19980421

OTHER SOURCE(S): MARPAT 129:343418
GI



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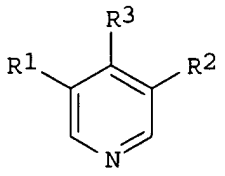

II

AB Title compds. (I; R1, R2 = H, Me; R3 = H, alkoxy, OCH2CF3, cyano, halo, acetoxy, aryloxy, electron withdrawing group; R4 = alkyl, acyl, amide, alkoxycarbonyl, aryloxycarbonyl, CO2H, PhOCH2, CH2OH or equivs.), were prepared by reaction of compds. (II; variables as above) under free radical conditions with R4 radical. Thus, 4-chloro-3,5-dimethylpyridine (preparation given) in aqueous H2SO4/PhMe was treated with a mixture prepared from Et pyruvate and 30-35% aqueous H2O2 and with an aqueous solution of iron sulfate to give >90% Et 4-chloro-3,5-dimethylpyridine-2-carboxylate. This was converted to 3,5-dimethyl-2-hydroxymethyl-4-methoxypyridine.
NO HIGHLIGHTING INFORMATION PRESENT

L1 ANSWER 25 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 123:228183 CASREACT
TITLE: New process for the synthesis of a 2-(2-pyridylmethylsulfinyl)benzimidazole derivative [**lansoprazole**], and new intermediates prepared in the process.
INVENTOR(S): Buxade Vinas, antonio
PATENT ASSIGNEE(S): Laboratorios Vinas, S.A., Spain
SOURCE: Span., 15 pp.
CODEN: SPXXAD

10/646,059

DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2060541	A1	19941116	ES 1993-384	19930226
ES 2060541	B1	19951116		

PRIORITY APPLN. INFO.: ES 1993-384 19930226
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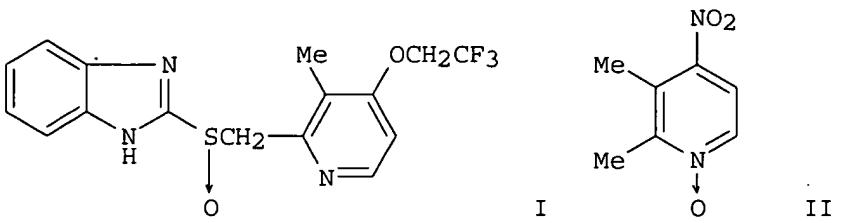
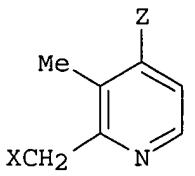
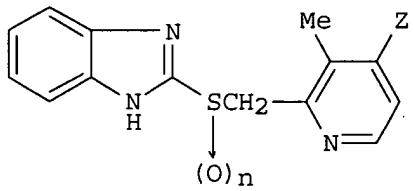


I

II



III



IV

AB The antisecretory agent **lansoprazole** (I) is prepared by a new, more economical, and less toxic process, in 3-4 steps starting from 2,3-dimethyl-4-nitropyridine N-oxide (II). For example, reaction of II with CCl3COCl in refluxing CHCl3, followed by NaOH in MeOH, and then workup and treatment with excess refluxing SOCl2, gave 55% 4-chloro-2-chloromethyl-3-methylpyridine [III; X = Z = Cl]. Reaction of III [X = Cl, Br; Z = halo, NO2] with 2-mercaptobenzimidazole and NaOH in aqueous MeOH gave >85% sulfides IV [Z = Cl, Br, NO2; n = 0]. Oxidation of the latter with potassium peroxymonosulfate (62-76%) or with H2O2 and Mo or V acetylacetonate catalysts (71-82%) gave IV [Z = Cl, Br, NO2; n = 1]. These reacted with CF3CH2OH and NaH in DMSO to give I in 72% (Z = Cl), 80% (Z = Br), or 48% (Z = NO2) yield.
NO HIGHLIGHTING INFORMATION PRESENT

L1 ANSWER 26 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 123:143645 CASREACT
TITLE: Improvements in the object of patent 9,102,594 for a process for the preparation of pyridine derivatives.
INVENTOR(S): Palomo Coll, Alberto
PATENT ASSIGNEE(S): Centro Genesis para la Investigacion S.L., Spain
SOURCE: Span., 15 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2058027	A1	19941016	ES 1993-240	19930209
ES 2058027	B1	19950516		

PRIORITY APPLN. INFO.: ES 1991-2590 19911121
OTHER SOURCE(S): MARPAT 123:143645
GI For diagram(s), see printed CA Issue.
AB In the title-referenced process for the preparation of pyridine N-oxides I and pyridinemethanols II [R2, R3 = H, Me, OMe; R4 = CH2CF3, Et, iso-Pr, (CH2)3OMe], the improvement is characterized by reaction, in a solvent, of the reactive intermediate salts III or IV [D = variable-valence element; a, b = 0 or integer, with (a+b)>0] with a corresponding alc. derivative D(OR4)c-M+ [V; M = Lewis acid, protonated organic base, Si derivative]. Elements functioning as D include Pd, P, S, B, and Br. The method is applicable to preparation of intermediates for antiulcer agents, especially **lansoprazole.** For example, 0.4 mL PBr3 was heated with 5 mL CF3CH2OH at 70° until formed HBr was eliminated (solution A). Meanwhile, 3 g 85% KOH was added to 10 mL CF3CH2OH at 5°, with the temperature rising to 20-25° (solution B). Upon dissoln. of KOH, solution A was added to solution B, followed by 2.5 g 2,3-dimethyl-4-nitropyridine N-oxide. Refluxing of the mixture for 2 h 25 min gave complete reaction to a single product by TLC, namely 2,3-dimethyl-4-(2,2,2-trifluoroethoxy)pyridine N-oxide (VI). Addnl. examples show preparation of VI using SCl2 or Br2 in place of PBr3. Evidence for the existence of the denitro-supercations in III and IV, and the superanions in V, is described.
NO HIGHLIGHTING INFORMATION PRESENT

L1 ANSWER 27 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 123:32966 CASREACT
TITLE: Improvements in the object of patent 9102594 for a process for preparation of pyridine derivatives.
INVENTOR(S): Palomo Coll, Alberto
PATENT ASSIGNEE(S): Centro Genesis para la Investigacion S.L., Spain
SOURCE: Span., 11 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2067407	A1	19950316	ES 1993-935	19930504
ES 2067407	B1	19960416		
ES 2036948	A1	19930601	ES 1991-2594	19911121
ES 2036948	B1	19940901		

PRIORITY APPLN. INFO.: ES 1991-2594 19911121
OTHER SOURCE(S): MARPAT 123:32966
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

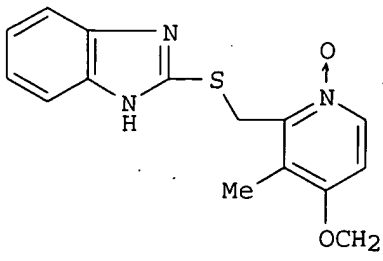
AB The preparation of compds. I [Z = OR4; X = CH, N; R1 = H, OMe, OCHF2, OCH2CF3, OPr-iso, OBu-iso, cyclopropylmethoxy; R2, R3 = H, Me, OMe; R4 = CH2CF3, Et, Pr-iso, Me, (CH2)3OMe], which include antiulcer agents such as

lansoprazole, according to Spanish patent 9,102,594, is improved. The preparation involves: (1) "allylic" chlorination of the Me group of pyridine N-oxides II [Z = NO2, halo, Me, OMe]; (2) condensation of the products (e.g., III) with a corresponding thiol IV; (3) oxidation of the resultant thioether to give I [Z = same]; and (3) conversion of the latter I to target compds. I [Z = OR4]. The improvement involves conducting the chlorination of II (step 1) using either: (a) CCl3COCl in the presence of γ-picoline and HCl to give III; or (b) trichloroisocyanuric acid in the presence of benzamide, followed by deoxygenation of the resultant N-oxide, to give III. For example, chlorination of 2,3-dimethyl-4-nitropyridine N-oxide using method (b) in refluxing CHCl3 gave 84% 2-(chloromethyl)-3-methyl-4-nitropyridine N-oxide, which was deoxygenated by SCl2 in CH2Cl2 at 0 to -10° to give 100% 2-(chloromethyl)-3-methyl-4-nitropyridine hydrochloride. Reaction of the latter with 2-mercaptobenzimidazole in Me2CO under catalysis by DIMAC at 30-35° gave 90% thioether V.
NO HIGHLIGHTING INFORMATION PRESENT

L1 ANSWER 28 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 122:290859 CASREACT
TITLE: Process and catalysts for the preparation of 2-[[(1H-benzimidazol-2-yl)thio]methyl]-3-methyl-4-(2,2,2-trifluoroethoxy)pyridinium N-oxide as an intermediate for **lansoprazole** bulk manufacture
INVENTOR(S): Monserrat Vidal, Carlos; Serra, Marcia, Xavier
PATENT ASSIGNEE(S): Laboratorios S.A.L.V.A.T., S.A., Spain
SOURCE: Span., 13 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2063705	A1	19950101	ES 1993-1312	19930614
ES 2063705	B1	19950716		

PRIORITY APPLN. INFO.: ES 1993-1312 19930614
GI



I

AB The title compound, I, is prepared from 2,3-dimethyl-4-nitropyridinium N-oxide in 3 steps and is used as an intermediate for the industrial-scale preparation of **lansoprazole**.
NO HIGHLIGHTING INFORMATION PRESENT

L1 ANSWER 29 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 122:133189 CASREACT
TITLE: Preparation of omeprazole and **lansoprazole** via oxidation of amide thioether, hydrolysis of sulfinyl amide, and decarboxylation of sulfinyl carboxylate
INVENTOR(S): Slemon, Clarke; Macel, Bob
PATENT ASSIGNEE(S): Torcan Chemical Ltd., Can.
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5374730	A	19941220	US 1993-145572	19931104
US 5470983	A	19951128	US 1994-276378	19940718
CA 2170250	AA	19950511	CA 1994-2170250	19940817
CA 2170250	C	19970916		
WO 9512590	A1	19950511	WO 1994-CA452	19940817
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9474875	A1	19950523	AU 1994-74875	19940817
EP 724582	A1	19960807	EP 1994-924662	19940817
EP 724582	B1	20011010		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09504530	T2	19970506	JP 1994-512922	19940817
JP 2966097	B2	19991025		
AT 206707	E	20011015	AT 1994-924662	19940817
US 5502195	A	19960326	US 1994-345725	19941122

PRIORITY APPLN. INFO.: US 1993-145572 19931104
US 1994-276378 19940718
WO 1994-CA452 19940817
OTHER SOURCE(S): MARPAT 122:133189
GI

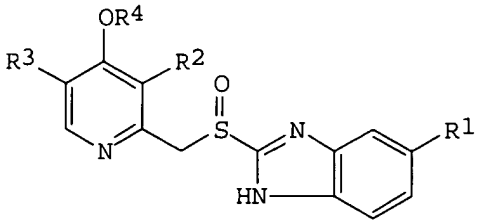
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A process for preparing a pyridine-benzimidazole compound of formula I in which either (a) R and R1 are each Me and R2 is methoxy;, or (b) R is 1,1,1-trifluoroethyl and R1 and R2 are both hydrogen, which comprises oxidizing an amide of the formula (II) to produce the corresponding amide sulfinyl compound, subjecting the amide sulfinyl compound so formed to alkaline hydrolysis to form a sulfinyl carboxylate, or a salt thereof, of formula (III) in which X is an alkali metal, Y is hydrogen or a metal, or X and Y together represent a divalent alkaline earth metal; and decarboxylating the sulfinyl carboxylate of formula (III) to form the sulfoxide compound of formula (I), the groups R, R1, and R2 in formulas (II) and (III) having the same meanings as given above, and the group R4 in formula (II) representing hydrogen, lower alkyl or aryl-lower alkyl, optionally further substituted by other functionality to assist in the hydrolysis step.
NO HIGHLIGHTING INFORMATION PRESENT

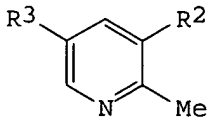
L1 ANSWER 30 OF 30 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 120:107017 CASREACT
TITLE: Process for preparation of benzimidazole-containing derivatives of pyridine [e.g., **lansoprazole**]
INVENTOR(S): Palomo Coll, Alberto
PATENT ASSIGNEE(S): Centro Genesis para la Investigacion S.L., Spain
SOURCE: Span., 34 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2036948	A1	19930601	ES 1991-2594	19911121
ES 2036948	B1	19940901		
ES 2066701	A1	19950301	ES 1993-64	19930115
ES 2066701	B1	19951201		
ES 2067407	A1	19950316	ES 1993-935	19930504
ES 2067407	B1	19960416		
ES 2105953	A1	19971016	ES 1994-2419	19941124
ES 2105953	B1	19980701		

PRIORITY APPLN. INFO.: ES 1991-2594 19911121
OTHER SOURCE(S): MARPAT 120:107017
GI



I



II

AB Pyridine derivs. I [X = CH, N; R1 = H, OMe, OCHF2, OCH2CF3, OCHMe2, OCH2CHMe2, cyclopropylmethoxy; R2, R3 = H, Me, OMe; R4 = CH2CF3, Et, CHMe2, Me, (CH2)3OMe; except case of X = CH, R1 = OMe, R2-R4 = Me], used as antiulcer agents (no data), are prepared in a min. of 7 steps from simple pyridines II by several synthetic variations. For example, 2,3-dimethylpyridine underwent N-oxidation and 4-nitration (95%), monochlorination of the 2-Me group (95%), N-reduction and conversion to the HCl salt (87%), thioetherification of the CH2Cl group with 2-mercaptobenzimidazole (87%), Pd(PPh3)4-catalyzed displacement of nitro by CF3CH2OH (90%), and S-oxidation (75%) to give I [X = CH, R1 = R3 = H, R2 = Me, R4 = CH2CF3], i.e. **lansoprazole.**
NO HIGHLIGHTING INFORMATION PRESENT

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